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WHAT IS CLAIMED IS:

1. A method for detecting or measuring Notch activation in a cell comprising detecting or measuring the expression of Notch on the surface of said cell, wherein the presence and amount of Notch on the surface indicates the presence and amount, respectively, of Notch activation.

2. The method according to claim 1 in which Notch on the cell surface is in the form of a heterodimer containing a reducing agent-sensitive linkage.

3. The method according to claim 2 in which the heterodimer consists of an amino-terminal fragment of full-length Notch terminating between the epidermal growth factor-like repeat domain and the transmembrane domain of full-length Notch, and a carboxy-terminal fragment of full-length Notch with its amino terminus situated between the epidermal growth factor-like repeat domain and the transmembrane domain.

4. The method according to claim 1 in which said detecting or measuring is carried out by a method comprising contacting the cell in intact form with a molecule that binds to the extracellular portion of Notch under conditions conducive to specific binding; and detecting any binding of the molecule to the cell that occurs.

5. The method according to claim 4 in which the molecule is an anti-Notch antibody or a binding region thereof.

6. The method according to claim 4 in which the molecule is Delta or Serrate or a binding region thereof.

7. The method according to claim 5 in which the antibody or binding region thereof is labelled with a

fluorescent label, and binding of the antibody to the cell is detected or measured by fluorescent activated cell sorting.

8. The method according to claim 1 in which said detecting or measuring is carried out by a method comprising (a) contacting the cell with a reagent that binds to or reacts with cell surface proteins under conditions conducive to such binding or reaction; and (b) detecting any such binding to or reaction with Notch.

9. The method according to claim 8 in which the reagent is labeled.

10. The method according to claim 8 in which said detecting is carried out by a method comprising contacting the cell with a labeled specific binding partner to the reagent.

11. The method according to claim 9 or 10 in which the detecting of any such binding or reaction in step (b) is carried out by western blotting or immunoprecipitation, using an anti-Notch antibody.

12. The method according to claim 1 in which the cell is a cell recombinantly expressing Notch.

13. The method according to claim 12 in which the cell is a cell of an animal containing and expressing a Notch transgene.

14. The method according to claim 13 in which the animal is a *Drosophila*.

15. The method according to claim 13 in which the animal is a *C. elegans*.

16. The method according to claim 1 in which the Notch is a mammalian Notch.

17. The method according to claim 1 in which the Notch is a human Notch.

18. The method according to claim 1 in which the detecting or measuring is carried out by (a) labeling proteins expressed on the cell surface; and (b) detecting the label of step (a) on Notch.

19. The method according to claim 18 in which the label of step (a) is biotin or ^{125}I.

20. The method according to claim 18 in which Notch is isolated by binding to an anti-Notch antibody prior to step (b).

21. The method according to claim 18 in which Notch is isolated by binding to a Notch ligand prior to step (b).

22. The method according to claim 21 in which the Notch ligand is selected from the group consisting of Delta and Serrate.

23. The method according to claim 1 in which the detecting or measuring is carried out by contacting a first plurality of said cell with a second plurality of cells expressing a Notch ligand on their surfaces; and measuring cell aggregation between cells in said first plurality and cells in second plurality.

24. The method according to claim 23 in which the Notch ligand is Delta or Serrate.

25. A method for detecting or measuring Notch activation in a cell comprising detecting or measuring the expression of one or more Notch cleavage products selected from the group consisting of N^{EC} and N^{TM}.

26. The method according to claim 25 in which the one or more Notch cleavage products are detected by immunoprecipitation or western blotting with an anti-Notch antibody.

27. A method for detecting or measuring Notch activation in a cell comprising detecting or measuring one or more fragments of Notch selected from the group consisting of an amino-terminal fragment of full-length Notch terminating between the epidermal growth factor-like repeat domain and the transmembrane domain of full-length Notch, and a carboxy-terminal fragment of full-length Notch with its amino terminus situated between the epidermal growth factor-like repeat domain and the transmembrane domain.

28. A method for detecting or measuring Notch activation in a cell comprising detecting or measuring one or more fragments of Notch selected from the group consisting of Notch fragments having a molecular weight of about 270, 200, 170, 140, 110, 100, 90 and 85 kilodaltons.

29. The method according to claim 28 which comprises detecting a pattern of Notch cleavage products as shown in Figure 10A or 10B.

30. The method according to claim 27 in which the fragments are about 180 kilodaltons and 110 kilodaltons, respectively.

31. A method for detecting or measuring Notch activation in a cell comprising detecting or measuring a

Notch heterodimer containing a reducing agent-sensitive linkage.

32. A method for identifying a modulator of Notch activation comprising providing a cell with a candidate modulator molecule and detecting or measuring the amount of Notch on the surface of the cell, in which a difference in the presence or amount compared to a cell not contacted with the candidate molecule indicates that the candidate molecule modulates Notch activation.

33. The method according to claim 32 in which the candidate molecule decreases the amount of Notch on the surface of the contacted cell, thereby being a candidate inhibitor of Notch activation.

34. The method according to claim 32 in which the candidate molecule increases the amount of Notch on the surface of the contacted cell, thereby being a candidate agonist of Notch activation.

35. The method according to claim 32 in which the candidate molecule decreases the amount of Notch on the surface of the contacted cell in the presence of a Notch agonist, thereby being a candidate antagonist of Notch activation.

36. The method according to claim 32 in which Notch on the cell surface is in the form of a heterodimer containing a reducing agent-sensitive linkage.

37. The method according to claim 36 in which the heterodimer consists of an amino-terminal fragment of full-length Notch terminating between the epidermal growth factor-like repeat domain and the transmembrane domain of full-length Notch, and a carboxy-terminal fragment of full-length Notch with its amino terminus situated between the epidermal

growth factor-like repeat domain and the transmembrane domain.

38. The method according to claim 32 in which said detecting or measuring is carried out by a method comprising (a) contacting the cell in intact form with a molecule that binds to the extracellular portion of Notch under conditions conducive to specific binding; and (b) detecting any binding of the molecule to the cell that occurs.

39. The method according to claim 38 in which the molecule is an anti-Notch antibody or a binding region thereof.

40. The method according to claim 38 in which the molecule is Delta or Serrate or a binding region thereof.

41. The method according to claim 39 in which the antibody or binding region thereof is labelled with a fluorescent label, and binding of the antibody to the cell is detected or measured by fluorescent activated cell sorting.

42. The method according to claim 32 in which said detecting or measuring is carried out by a method comprising (a) contacting the cell with a reagent that binds to or reacts with cell surface proteins under conditions conducive to such binding or reaction; and (b) detecting any such binding to or reaction with Notch.

43. The method according to claim 42 in which the reagent is labeled.

44. The method according to claim 42 in which said detecting is carried out by a method comprising contacting the cell with a labeled specific binding partner to the reagent.

45. The method according to claim 43 or 44 in which the detecting of any such binding or reaction in step (b) is carried out by western blotting or immunoprecipitation, using an anti-Notch antibody.

46. The method according to claim 32 in which the cell is a cell recombinantly expressing Notch.

47. The method according to claim 46 in which the cell is a cell of an animal containing and expressing a Notch transgene.

48. The method according to claim 47 in which the animal is a *Drosophila*.

49. The method according to claim 47 in which the animal is a *C. elegans*.

50. The method according to claim 32 in which the Notch is a mammalian Notch.

51. The method according to claim 32 in which the Notch is a human Notch.

52. The method according to claim 32 in which the detecting or measuring is carried out by (a) labeling proteins expressed on the cell surface; and (b) detecting the label of step (a) on Notch.

53. The method according to claim 52 in which the label of step (a) is biotin or ^{125}I.

54. The method according to claim 32 in which Notch is isolated by binding to an anti-Notch antibody prior to step (b).

55. The method according to claim 32 in which Notch is isolated by binding to a Notch ligand prior to step (b).

56. The method according to claim 55 in which the Notch ligand is selected from the group consisting of Delta and Serrate.

57. The method according to claim 32 in which the detecting or measuring is carried out by contacting a first plurality of said cell with a second plurality of cells expressing a Notch ligand on their surfaces; and measuring cell aggregation between cells in said first plurality and cells in second plurality.

58. The method according to claim 57 in which the Notch ligand is Delta or Serrate.

59. A method for identifying a modulator of Notch activation comprising providing a cell with a candidate modulator molecule and detecting or measuring the expression by the cell of one or more Notch cleavage products selected from the group consisting of N^{EC} and N^{TM}, in which a difference in the presence or amount of said one or more cleavage products compared to a Notch cell not contacted with the candidate molecule indicates that the molecule modulates Notch activity.

60. A method for identifying a modulator of Notch activation comprising contacting a cell with a candidate modulator molecule and detecting or measuring the amount of the expression by the cell of one or more fragments of Notch selected from the group consisting of an amino-terminal fragment of full-length Notch terminating between the epidermal growth factor-like repeat domain and the transmembrane domain of full-length Notch, and a carboxy-terminal fragment of full-length Notch with its amino

terminus situated between the epidermal growth factor-like repeat domain and the transmembrane domain; in which a difference in the presence or amount of said one or more fragments compared to a Notch cell not contacted with the candidate molecule indicates that the molecule modulates Notch activity.

61. A method for identifying a modulator of Notch activation comprising contacting a cell with a candidate modulator molecule and detecting or measuring the expression by the cell of one or more fragments of Notch selected from the group consisting of Notch fragments having a molecular weight of about 270, 200, 170, 140, 110, 100, 90 and 85 kilodaltons, in which a difference in the presence or amount of said one or more fragments compared to a Notch cell not contacted with the candidate molecule indicates that the molecule modulates Notch activity.

62. A method for identifying a modulator of Notch activation comprising contacting a cell with a candidate modulator molecule and detecting or measuring the amount of the expression by the cell of a pattern of Notch cleavage products as shown in Figure 10A or 10B, in which a difference in the presence or amount of said pattern compared to a Notch cell not contacted with the candidate molecule indicates that the molecule modulates Notch activity.

63. A method for identifying a modulator of Notch activation comprising contacting a cell with a candidate modulator molecule and detecting or measuring the amount of the expression by the cell of one or more Notch fragments of about 180 kilodaltons and about 110 kilodaltons, respectively, in which a difference in the presence or amount of the fragments compared to a Notch cell not contacted with the candidate molecule indicates that the molecule modulates Notch activity.

64. A method for identifying a modulator of Notch activation comprising contacting a cell with a candidate modulator molecule and detecting or measuring the amount of the expression by the cell of a Notch heterodimer containing a reducing agent-sensitive linkage, in which a difference in the presence or amount of the heterodimer compared to a Notch cell not contacted with the candidate molecule indicates that the molecule modulates Notch activity.

65. The method according to claim 59 in which the candidate molecule decreases said expression, thereby being a candidate inhibitor of Notch activation.

66. The method according to claim 59 in which the candidate molecule increases said expression, thereby being a candidate agonist of Notch activation.

67. The method according to claim 59 in which the Notch cleavage products are detected by contacting a protein-containing sample from the cell with an anti-Notch antibody or a binding region thereof under conditions conducive to immunospecific binding, and separating by size any components that bind.

68. A method for identifying a modulator of Notch activation comprising contacting a candidate modulator molecule with a full length Notch in the presence of a composition comprising cellular proteins, under conditions conducive to cleavage of the full-length Notch by one or more components of the composition and detecting or measuring the amount of Notch cleavage products N^{EC} and N^{TM} that result, in which a difference in the presence or amount of said Notch cleavage products compared to a full-length Notch in presence of said composition not contacted with the candidate molecule indicates that the molecule modulates Notch activity.

69. The method according to claim 68 in which the composition is a cell lysate made from cells which recombinantly express Notch.

70. The method according to claim 68 in which the composition is a cell lysate made from cells which endogenously express Notch.

71. A method for identifying a modulator of Notch activation comprising contacting a candidate modulator molecule with a full length Notch in the presence of a composition comprising cellular proteins, under conditions conducive to cleavage of the full-length Notch by one or more components of the composition and detecting or measuring one or more fragments of Notch selected from the group consisting of an amino-terminal fragment of full-length Notch terminating between the epidermal growth factor-like repeat domain and the transmembrane domain of full-length Notch, and a carboxy-terminal fragment of full-length Notch with its amino terminus situated between the epidermal growth factor-like repeat domain and the transmembrane domain, that result, in which a difference in the presence or amount of said one or more Notch fragments compared to a full-length Notch in presence of said composition not contacted with the candidate molecule indicates that the molecule modulates Notch activity.

72. A method for identifying a modulator of Notch activation comprising contacting a candidate modulator molecule with a full length Notch in the presence of a composition comprising cellular proteins, under conditions conducive to cleavage of the full-length Notch by one or more components of the composition and detecting or measuring the amount of one or more fragments of Notch selected from the group consisting of Notch fragments having a molecular weight of about 270, 200, 170, 140, 110, 100, 90 and 85 kilodaltons, that result, in which a difference in the presence or amount

of said one or more Notch fragments compared to a full-length Notch in presence of said composition not contacted with the candidate molecule indicates that the molecule modulates Notch activity.

73. A method for identifying a modulator of Notch activation comprising contacting a candidate modulator molecule with a full length Notch in the presence of a composition comprising cellular proteins, under conditions conducive to cleavage of the full-length Notch by one or more components of the composition, and detecting or measuring the amount of a pattern of Notch cleavage products as shown in Figure 10A or 10B that result, in which a difference in the presence or amount of said pattern compared to a full-length Notch in presence of said composition not contacted with the candidate molecule indicates that the molecule modulates Notch activity.

74. A method for identifying a modulator of Notch activation comprising contacting a candidate modulator molecule with a full length Notch in the presence of a composition comprising cellular proteins, under conditions conducive to cleavage of the full-length Notch by one or more components of the composition, and detecting or measuring the amount of one or more Notch fragments of about 180 kilodaltons and about 110 kilodaltons, respectively, that result, in which a difference in the presence or amount of said one or more Notch fragments compared to a full-length Notch in presence of said composition not contacted with the candidate molecule indicates that the molecule modulates Notch activity.

75. A method for identifying a modulator of Notch activation comprising contacting a candidate modulator molecule with a full length Notch in the presence of a composition comprising cellular proteins, under conditions conducive to cleavage of the full-length Notch by one or more

components of the composition, and detecting or measuring the amount of a Notch heterodimer containing a reducing agent-sensitive linkage that results, in which a difference in the presence or amount of said heterodimer compared to a full-length Notch in the presence of said composition not contacted with the candidate molecule indicates that the molecule modulates Notch activity.

76. A purified heterodimeric form of Notch comprising Notch fragments tethered together through a reducing agent-sensitive linkage.

77. The heterodimeric form of claim 76 which comprises an about 180 kilodalton subunit and an about 110 kilodalton subunit.

78. The heterodimeric form of claim 76 in which the heterodimer consists of an amino-terminal fragment of full-length Notch terminating between the epidermal growth factor-like repeat domain and the transmembrane domain of full-length Notch, and a carboxy-terminal fragment of full-length Notch with its amino terminus situated between the epidermal growth factor-like repeat domain and the transmembrane domain.

79. The method according to claim 32 in which said providing is carried out by intracellular expression of said candidate molecule.

80. A purified amino-terminal fragment of full length Notch terminating between the epidermal growth factor-like repeat region and the transmembrane domain.

81. A pharmaceutical composition comprising the purified heterodimeric form of claim 76, and a pharmaceutically acceptable carrier.

82. A pharmaceutical composition comprising the purified fragment of claim 80, and a pharmaceutically acceptable carrier.

83. A pharmaceutical composition comprising a purified carboxy-terminal fragment of full length Notch with its amino-terminus situated between the epidermal growth factor-like repeat region and the transmembrane domain, and a pharmaceutically acceptable carrier.

84. A kit comprising in one or more containers: (a) a purified heterodimer comprising Notch fragments tethered together through a reducing agent-sensitive linkage; (b) an amino-terminal fragment of full-length Notch terminating between the epidermal growth factor-like repeat domain and the transmembrane domain; and (c) a carboxy-terminal fragment of full-length Notch with its amino terminus situated between the epidermal growth factor-like repeat domain and the transmembrane domain.

85. The method according to claim 1 in which the cell is contained in an animal.

86. The method according to claim 2, 3, 31, 36, 37, 64 or 75 in which the reducing agent-sensitive linkage is a non-covalent, metal ion-dependent sensitive linkage.

87. The heterodimeric form of claim 76 or 78 in which the reducing agent-sensitive linkage is a non-covalent, metal ion-dependent sensitive linkage.

88. The method according to claim 3, 27, 37, 60 or 71 in which the amino-terminal fragment of full-length Notch terminates between the Lin-12/Notch repeats and the transmembrane domain, and the carboxy-terminal fragment of full-length Notch has its amino terminus situated between the Lin-12/Notch repeats and the transmembrane domain.

89. The heterodimeric form of claim 78 in which the amino-terminal fragment of full-length Notch terminates between the Lin-12/Notch repeats and the transmembrane domain, and the carboxy-terminal fragment of full-length Notch has its amino terminus situated between the Lin-12/Notch repeats and the transmembrane domain.

90. The amino-terminal fragment of claim 80 in which the fragment terminates between the Lin-12/Notch repeats and the transmembrane domain.

91. The carboxy-terminal fragment of claim 83 in which the fragment has an amino-terminus situated between the Lin-12/Notch repeats and the transmembrane domain.

92. The kit according to claim 84 in which the amino-terminal fragment of full-length Notch terminates between the Lin-12/Notch repeats and the transmembrane domain, and the carboxy-terminal fragment of full-length Notch has its amino terminus situated between the Lin-12/Notch repeats and the transmembrane domain.